

**FORM PTO-1449**  
**INFORMATION DISCLOSURE STATEMENT**

<b>SERIAL NO.</b>	<b>10/595,932</b>
<b>FILING DATE</b>	<b>May 19, 2006</b>
<b>APPLICANT</b>	<b>Mercep et al.</b>
<b>GROUP</b>	<b>1617</b>
<b>EXAMINER</b>	<b>K.D. Carter</b>
<b>ATTORNEY DOCKET NO.</b>	<b>PLP527USw</b>

**U.S. PATENT DOCUMENTS**

Examiner Initials	Patent Number	Issue Date	Name	Class	Subclass	Filing Date If Appropriate
/K.C./	3,773,940	Nov. 20, 1973	Schindler et al.			
/K.C./	3,781,294	Dec. 25, 1973	Lombardino			
/K.C./	3,859,439	Jan. 7, 1975	Blattner et al.			
/K.C./	3,894,032	July 8, 1975	Remy			
/K.C./	3,974,285	Aug. 10, 1976	Remy			
/K.C./	4,044,143	Aug. 23, 1977	Remy			
/K.C./	4,112,110	Sept. 15, 1978	Blattner			
/K.C./	4,267,184	May 12, 1981	Cherkofsky et al.			
/K.C./	4,267,190	May 12, 1981	Cherkofsky et al.			
/K.C./	4,271,179	June 2, 1981	van der Burg			
/K.C./	5,917,057	June 29, 1999	Hamer et al.			
/K.C./	2003/0153750	Aug. 14, 2003	Mladen et al.			
/K.C./	2005/0148578	July 7, 2005	Mercep et al.			

Continue on page

**FOREIGN PATENT DOCUMENTS**

	Document Number	Publication Date	Country	Class	Subclass	Translation Yes   No
/K.C./	14 EP 0125484	Nov. 21, 1984	EUROPE			
/K.C./	15 EP 0357126	Mar. 7, 1990	EUROPE			
/K.C./	16 EP 0372445	June 13, 1990	EUROPE			
/K.C./	17 WO 91/18885	Dec. 12, 1991	WIPO			
/K.C./	18 WO 98/54186	Dec. 3 1998	WIPO			
/K.C./	19 WO 99/00355	Jan. 7, 1999	WIPO			X Abstract
/K.C./	20 WO 03/084961	Oct. 16, 2003	WIPO			
/K.C./	21 WO 03/097649	Nov. 27, 2003	WIPO			
/K.C./	22 WO 03/099823	Dec. 4, 2003	WIPO			
/K.C./	23 HR 20000310	Feb. 28, 2002	CROATIA			X
/K.C./	24 HR 20020453	May 23, 2002	CROATIA			X

Continue on page

**OTHER DOCUMENTS (Including Author, Title, Journal-Date, Page Number, Etc.)**

/K.C./	25	Ackermann L., Harvima I.T. "Mast cells of psoriatic and atopic dermatitis skin are positive for TNF- $\alpha$ and their degranulation is associated with expression of ICAM-1 in the epidermis." <i>Arch. Dermatol. Res.</i> 1998, 290:353-359.
/K.C./	26	Aderka, D. "Role of tumor necrosis factor in the pathogenesis of intravascular conglutopathy of sepsis: potential new therapeutic implications." <i>Isr. J. Med. Sci.</i> , 1991, 27:52-60.
/K.C./	27	Arrieta O, et al. "Protective effect of pentoxifylline plus thalidomide against septic shock in mice." <i>Int. J. Exp. Pathol.</i> 1999, 80(1):11-16.
/K.C./	28	Badger A.M. et al. "Beneficial effects of the phosphodiesterase inhibitors BRL 61063, pentoxifylline, and rolipram in a murine model of endotoxin shock." <i>Circ. Shock</i> 1994 44(4):188-195.
/K.C./	29	Badger et al. "Pharmacological profile of SB 203580, a selective inhibitor of cytokine suppressive binding protein/p38 kinase, in animal models of arthritis, bone resorption, endotoxin shock and immune function." <i>J. Pharmac. Env. Therap.</i> , 1996, 279(3):1453-1461.
/K.C./	30	Becker et al. "Photochemistry of the Anthracene Chromophore: Novel Isomerization of 1-(9-Anthryl)-2-Benzoethylenes." <i>Tetrahedron Lett.</i> , 1985, 26(12):1589-1592.
/K.C./	31	Bennett et al. "Reaction of 5-acetyl-10, didehydro-5H-dibenzo[b,f] azepine with pyrrole, N-methylpyrrole, imadazole and n-methylimidazole: cycloaddition versus Michael addition." <i>J. Heterocycl. Chem.</i> , 1994, 31:293-296.

/K.C./	32	Bissonnette E. Y. et al. "Inhibition of tumour necrosis factor-alpha (TNF-alpha) release from mast cells by the anti-inflammatory drugs, sodium cromoglycate and nedocromil sodium." <i>Clin. Exp. Immunol.</i> 1995, 102:78-84.
/K.C./	33	Bresnihan. "Treatment with recombinant human interleukin-1 receptor antagonist (rhIL-1ra) in rheumatoid arthritis (RA); results of randomized double-blind, placebo-controlled multicenter trial." <i>Arthrit. Rheum.</i> , 1996, 39:73.
/K.C./	34	Cagniant, C.R. Hebd. Sceances Acad. Sci., 1976, 283:683-686
/K.C./	35	Carswell et al. "An endotoxin-induced serum factor that causes necrosis of tumors." <i>Proc. Natl. Acad. Sci. U.S.A.</i> , 1975, 72:3666-3670.
/K.C./	36	Chapman P.T. et al. "Endothelial activation in monosodium urate monohydrate crystal-induced inflammation: in vitro and in vivo studies on the roles of tumor necrosis factor alpha and interleukin-1." <i>Arthritis Rheum.</i> , 1997, 40:955-965.
/K.C./	37	Cheung A. T. et al. "An in vivo model for elucidation of the mechanism of tumor necrosis factor-alpha (TNF-alpha)-induced insulin resistance: evidence for differential regulation of insulin signaling by TNF-alpha." <i>Endocrinology</i> , 1998, 139:4928-4935.
/K.C./	38	Collier L., et al. "The abdominal constriction response and its suppression by analgesic drugs in the mouse." <i>Br. J. Pharmac. Chemother.</i> , 1968, 32:295-310
/K.C./	39	Corral L., et al. "Differential Cytokine Modulation and T Cell Activation by Two Distinct Classes of Thalidomide Analogues That are Potent Inhibitors of TNF- $\alpha$ ." <i>The Journal of Immunology</i> 1999, 163:380-386.
/K.C./	40	Dibbs Z, et al. "Cytokines in heart failure: pathogenetic mechanisms and potential treatment." <i>Proc. Assoc. Am. Physicians</i> , 1999, 111:423-428.
/K.C./	41	Di Francia M. et al. "Tumor necrosis factor-alpha levels and weight loss in chronic obstructive pulmonary disease." <i>AM. J. Respir. Crit. Care Med.</i> 1994, 150:1453-1455.
/K.C./	42	Dinarello. "An update on human interleukin-1: From molecular biology to clinical relevance." <i>J. Clinical Immunology</i> , 1985, 5:287.
/K.C./	43	Dinarello. "Interleukin-1." <i>Rev. Infect. Disease</i> , 1984, 6(1):51-95.
/K.C./	44	Duong D.J. et al. "American experience with lowdose thalidomide therapy for severe cutaneous lupus erythematosus." <i>Arch. Dermatol.</i> 1999 135 (9):1079-1087.
/K.C./	45	Egido J. et al. "Role of tumor necrosis factor-alpha in the pathogenesis of glomerular diseases." <i>Kidney Int. Suppl.</i> 1993, 39:59-64.
/K.C./	46	Elliot et al. "Randomised double-blind comparison of chimeric monoclonal antibody to tumor necrosis factor alpha (cA2) versus placebo in rheumatoid arthritis." <i>The Lancet</i> , 1994, 344:1105-1110.
/K.C./	47	M. Feldman et al. "Role of Cytokines in Rheumatoid Arthritis." <i>Annu. Rev. Immunol.</i> 1996 14:397-440.
/K.C./	48	Fukawa et al. "A method for evaluating analgesic agents in rats." <i>J. Pharmacol. Meth.</i> , 1980, 4:251-259.
/K.C./	49	Funke et al. "Physico-chemical properties and stability of trans-5-chloro-2-methyl-2,3,3a,12b-tetrahydro-1-dibenz[2,3;6,7]joxepin-4,5-cipyrrolidine Maleate." <i>Arzneim-Forsch.</i> , 1190, 40:536-539.
/K.C./	50	Gauldie J. et al. "Cytokines and pulmonary fibrosis." <i>Thorax</i> , 1993, 48:931-935.
/K.C./	51	Georgopoulos et al. "Transmembrane TNF is sufficient to induce localized tissue toxicity and chronic inflammatory arthritis in transgenic mice." <i>J. Inflamm.</i> , 1996, 46:86-97.
/K.C./	52	Gruschwitz, M., et al. "In situ Expression and Serum Levels of Tumor Necrosis Factor- $\alpha$ Receptors in Patients with Early Stages of Systemic Sclerosis." <i>Journal Rheumatology</i> 1997; 24:1936-43.
/K.C./	53	Heilig, B. et al. "Elevated TNF Receptor Plasma Concentrations in Patients with Rheumatoid Arthritis." <i>Clinical Investigation</i> 1992; 70:22-27.
/K.C./	54	Heilig B et al. "[Expression of TNF receptors in rheumatoid arthritis and ankylosing spondylitis]." [Article in German]. <i>Z Rheumatol.</i> 1993 Nov-Dec; 52(6):383-9.
/K.C./	55	Hotamisligil G.S., Spiegelman B.M. "Tumor necrosis factor alpha: a key component of the obesity-diabetes link." <i>Diabetes</i> , 1994, 43:1271-1278.
/K.C./	56	Huff, J.R. "HIV Protease: A novel chemotherapeutic target for AIDS." <i>Journal of Medicinal Chemistry</i> , 34(8), pgs. 2305-2314.
/K.C./	57	Iyer and Gopalachari. "Studies in Potential Antifertility Agents: Part VII - Synthesis of Dialkylaminoethyl Derivatives of 2,4,5-triphenylpyrroles & 2,4,5-triphenylfurans." <i>Indian J. Chem.</i> , 1973, 11:1260-1262.
/K.C./	58	Jones et al. "Antiestrogens. 2. Structure-activity studies in a series of 3-aryl-2-arylbenzo[b]thiophene derivatives leading to [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]-phenyl]methanone hydrochloride (LY156758), a remarkably effective estrogen antagonist with only minimal intrinsic estrogenicity." <i>J. Med. Chem.</i> , 1984, 27:1057-1066.
/K.C./	59	Kapadia S. et al. "The role of cytokines in the failing human heart." <i>Cardiol. Clin.</i> , 1998, 16:645-656.
/K.C./	60	Kefford et al. "Transgenic mice expressing human tumour necrosis factor: a predictive genetic model of arthritis." <i>EMBO J.</i> , 1991, 10:4025-4031.
/K.C./	61	King, F.D. "Bioisosteres, Conformational Restriction, and Pro-Drugs - Case History: An Example of a Conformational Restriction Approach." <i>Med. Chem.: Principle and Practice</i> (1994) p. 206-208.
/K.C./	62	Kluth D.C., Rees A.J. "Inhibiting inflammatory cytokines." <i>Semin. Nephrol.</i> 1996, 16:576-582.
/K.C./	63	Kopicova et al. "Potential Tetracyclic Neuroleptics: 12-(4-methylpiperazino)benzo[b]naphtho[2,3-f]theipin and its 12,13-dihydro Derivative." <i>Collect. Czech. Chem. Commun.</i> , 1975, 40:1960-1965.

/K.C./	64	Kopicova and Protiva. "Synthesis of 7-(4-methylpiperazino)-7,8-dihydrobenzo[b]naphtho[2,1-flthiepin and of Related Compunds." <i>Collect. Czech. Chem. Commun.</i> , 1974, 39:3147-3152.
/K.C./	65	Krakauer T, Stiles BG. "Pentoxifylline inhibits superantigen-induced toxic shock and cytokine release." <i>Clin Diagn Lab Immunol.</i> 1999 Jul;6(4):594-8.
/K.C./	66	Liedtke W. "Effective Treatment of Models of Multiple Sclerosis by Matrix Metalloproteinase Inhibitors." <i>An. of Neurology.</i> 1998, Vol. 44; 35-46.
/K.C./	67	Liu J.Y. et al. "TNF-alpha receptor knockout mice are protected from the fibroproliferative effects of inhaled asbestos fibers." <i>Am. J. Pathol.</i> , 1998, 153:1839-1847.
/K.C./	68	Main R.N, Taylor P.C. "Anti-Cytokine Therapy for Rheumatoid Arthritis." <i>Annu. Rev. Med.</i> 2000 51:207-229.
/K.C./	69	Martel-Pelletier J., Alaaeddine N, Pelletier JP. "Cytokines and their role in the pathophysiology of osteoarthritis." <i>From Biosci.</i> 1999 4:D694-703.
/K.C./	70	Matsukawa A, et al. "Analysis of the Cytokine Network Among Tumor Necrosis Factor $\alpha$ , Interleukin-1 $\beta$ , Interleukin-8 and Interleukin-1 Receptor Antagonist in Monosodium Urate Crystal-Induced Rabbit Arthritis." <i>Lab Invest.</i> 1998; 78:559-569.
/K.C./	71	Matioli and Ghia. "Omega-dialkylaminoalkyl ethers of phenyl-(5-substituted 1-phenyl-1H-pyrazol-4-yl)methanols with analgesic and anti-inflammatory activity." <i>J. Heterocyclic Chem.</i> , 1997, 34:963-968.
/K.C./	72	McHugh et al. "Preparation of 8-Hydroxy-3,4-dibenz[ <i>b,f</i> ]azepine. A Novel Heterocyclic Ring System." <i>J. Heterocycl. Chem.</i> , 1990, 27:1839-42.
/K.C./	73	Mori et al. "Photochemical reactions of anthracene-naphthalene bichromophoric systems linked by a three-carbon chain." <i>J. Chem. Soc., Perkin Trans. 2</i> , 1996, 1:113-119.
/K.C./	74	Mori et al. "Attenuation of collagen-induced arthritis in 55-kDa TNF receptor type 1 (TNFR1)-IgG1-treated and TNFR1-deficient mice." <i>J. Immunol.</i> , 1996, 157:3178-3182.
/K.C./	75	Noguchi, M., et al. "Secretion imbalance between Tumor Necrosis Factor and its inhibitor in inflammatory bowel disease." <i>Gut</i> 1998, 43:203-209.
/K.C./	76	Novacek et al. "Reaction of 8-chloro-10-phenylhydrazono-10, 11-dihydro-dibenzo[ <i>b,f</i> ]thepine with aromatic aldehydes." <i>Collection Czechoslov. Chem. Commun.</i> , 1976, Vol. 41, 785-787.
/K.C./	77	Nyondi-Bougon et al. "[4+2] - Cycloadditions of 3-Amino-4-imino-4 <i>h</i> -thieno[3,4- <i>c</i> ][1 <i>h</i> ]benzopyran with some Selected Dienophiles." <i>J. Chem Soc., Perkin Trans. 1</i> , 1994, 15:2191-2195.
/K.C./	78	Odeh M. "Role of Cytokines in Rheumatoid Arthritis." <i>Drugs News Perspect.</i> , II(6) 1998, 331-341.
/K.C./	79	Oliver S., et al. "The Effect of Thalidomide and 2 Analogs on Collagen Induced Arthritis." <i>Journal of Rheumatology</i> 1998; 25:964-9.
/K.C./	80	Olivera et al. "Dibenzoepino '4,5-d pyrazoles: a facile approach via the Ullman-ether reaction." <i>Tetrahedron Letters</i> , 2000, 41(22):4353-4360.
/K.C./	81	Peleman R.A., Kips J.C., Pauwels R.A. "Therapeutic activities of theophylline in chronic obstructive pulmonary disease." <i>Clin. Exp. Allergy</i> 1998 28 Supp 1, 3:53-56.
/K.C./	82	Pfeffer et al. "Mice deficient for the 55kD tumor necrosis factor receptor are resistant to endotoxic shock, yet succumb to L. monocytogenes infection." <i>Cell</i> , 1993, 73:457-467.
/K.C./	83	Piguet P.F. et al. "Expression and localization of tumor necrosis factor-alpha and its mRNA in idiopathic pulmonary fibrosis." <i>Am. J. Pathol.</i> 1993, 143:651-655.
/K.C./	84	Piguet P.F., Vesin C. "Treatment by human recombinant soluble TNF receptor of pulmonary fibrosis induced by bleomycin or silica in mice." <i>Eur. Respir. J.</i> , 1994, 7:515-518.
/K.C./	85	Reimund J. "In vitro effects of oxpentoxylline on Inflammatory Cytokine Release in Patients with Inflammatory Bowel Disease." <i>Gut</i> 1997, 40:475-480.
/K.C./	86	Ross S., et al. "Suppression of TNF $\alpha$ Expression, Inhibition of TH1 Activity and Amelioration of Collagen-Induced Arthritis by Rolipram." <i>Journal of Immunology</i> , 1997, 159:6253-6259.
/K.C./	87	Rutgeerts P. et al. "Efficacy and Safety of Retreatment with Anti-Tumor Necrosis Factor Antibody (Infliximab) to Maintain Remission in Crohn's Disease." <i>Gastroenterology.</i> , 1999, 117:761-769.
/K.C./	88	Sandborn W. and Hanauer S. "Antitumor Necrosis Factor Therapy for Inflammatory Bowel Disease; A review of Agents, Pharmacology, Clinical Results and Safety." <i>Inflammatory Bowel Diseases</i> 1999, 5(2):119-133.
/K.C./	89	Saricaoglu H. et al. "Prevention of nickel-induced allergic contact reactions with pentoxylline." <i>Contact Dermatitis</i> 1998, 39(5):244-247.
/K.C./	90	Sasayama S. et al. "New insights into the pathophysiological role for cytokines in heart failure." <i>Cardiovasc Res.</i> 1999, 42:557-564.
/K.C./	91	Schmidt H. et al. "Thalidomide inhibits TNF response and increases survival following endotoxin injection in rats." <i>J. Surg. Res.</i> 1996 63(1):143-146.
/K.C./	92	Schulz et al. "Synthese von 1,3a,3,12b-tetrahydro-dibenzo[ <i>b,f</i> ]pyrazolo[3,4-d]azepin-Derivativen." <i>Z. Chem.</i> 1988, 28:181-182.
/K.C./	93	Schweizer et al. "Combined automated writhing/motility test for testing analgesics." <i>Agents and Actions</i> , 1988, 23:29-31.
/K.C./	94	Shire, MG and Muller GW. "TNF- $\alpha$ inhibitors and rheumatoid arthritis." <i>Exp. Opin. Ther. Patents.</i> 1998 8(5): 531-544.
/K.C./	95	Stirling D. I. Semin. "Thalidomide and its impact in dermatology." <i>Cutan. Med. Surg.</i> 1998 17(4):231-242.

/K.C./	96	Sykes A.P.. et al. "The effect of an inhibitor of matrix metalloproteinases on colonic inflammation in a Eritriobenzenesulphonic acid rat model of inflammatory bowel disease." <i>Aliment Pharmacol Ther.</i> 1999, 13:1535-1542.
/K.C./	97	Taylor R. Multiple Sclerosis: A Rehabilitive Approach. 1998, 9, 3, 525-536. "Immunologic Aspects of Multiple Sclerosis."
/K.C./	98	Tochtermann et al. Ein neuer Zugang zu chiralen Tribenzo-cycloheptanen-(Tribenzo-[a.c.e]cyclohepten-) und Tribenzo[b,d]thiepin-S,S-dioxid-Derivaten". <i>Chem. Ber.</i> , 1968, 101:3122-3137.
/K.C./	99	Tomizawa S. et al. "TNF inhibitory activity in the urine of chronic renal failure patients with glomerulonephritis." <i>Nephron.</i> 1993, 63:111-112.
/K.C./	100	Tsujii et al. "Studies on Anti-Inflammatory Agents. VI. Synthesis and Pharmacological Properties of 2,3-Diarylthiophenes." <i>Chem. Pharm. Bull.</i> , 1998, 46(2):279-286.
/K.C./	101	Ueda et al. "The Synthesis of 10-(4-Methylpiprazino)dibenzo[b,f]thiepin and Related Compounds. Neurotropic and Psychotropic Agents." <i>Chem. Pharm. Bull.</i> , 1975, 23(10):2223-2231.
/K.C./	102	Van Assche and Rutgeerts. "Anti-TNF agents in Crohn's disease." <i>Exp. Opin. Invest. Drugs.</i> 2000, 9:103-111.
/K.C./	103	van den Berg, W.B. "Anti-Cytokine Therapy in Chronic Destructive Arthritis." <i>Arthritis Res</i> 2001, 3:18-26.
/K.C./	104	Vippagunta, S.R. et al. "Crystalline solids." <i>Advanced Drug Delivery Reviews.</i> 2001, 48(1):3-26.
/K.C./	105	Westacott C.J. et al. "Tumor necrosis factor alpha can contribute to focal loss of cartilage in osteoarthritis." <i>Osteoarthritis Cartilage</i> 2000 8(3):213-221.
/K.C./	106	Postmarketing Adverse Event Data for TNF-alpha Antagonists (October 23, 2001). Stephen A. Paget, MD < <a href="http://rheumatology.hss.edu/phys/specialreports/pagetttnf.asp">http://rheumatology.hss.edu/phys/specialreports/pagetttnf.asp</a> >
/K.C./	107	Green (Using TNF alpha technology to treat rheumatoid arthritis) Article (July/August 2004). < <a href="http://rheumatology.hss.edu/phys/specialreports/pagetttnf.asp">http://rheumatology.hss.edu/phys/specialreports/pagetttnf.asp</a> >
/K.C./	108	Centocor products (08/11/2004) < <a href="http://www.centocor.com/cgi-bin/site/products/prod_remicade.cgi">http://www.centocor.com/cgi-bin/site/products/prod_remicade.cgi</a> > is cited for the statement that>
/K.C./	109	"News & Notices: <a href="http://www.psoriasis.org/enbrel.approval.jan02.htm">http://www.psoriasis.org/enbrel.approval.jan02.htm</a> (7/30/2002).

Continue on page \_\_\_\_\_

EXAMINER	/Kendra Carter/	DATE CONSIDERED
07/01/2009		

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP § 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to the applicant.